REMARKS

The Office Action mailed November 30, 2004, has been received and reviewed. Newly added claims 57-126 were considered by the Office to be directed to a patentably distinct invention and were therefore withdrawn from prosecution (page 2 of the Office Action). As a result, applicants have reinstated former claims 21-34 and 36-46 as new claims 127-150 (*see*, page 2 of the Office Action mailed October 2, 2003, wherein Group II encompassed claims 20-46). Therefore, the Office has already acknowledged that new claims 127-150, which depend directly or indirectly from claim 20, are drawn to the elected invention.

Claims 20, 35, and 36 stand rejected under 35 U.S.C. § 112, first paragraph, for assertedly lacking sufficient written description. Claims 20, 35, and 36 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Plasterk *et al.*, in view of Vos *et al.*, Van Leunen *et al.* '94[1], Van Leunen *et al.* '93[2], Hackett *et al.* and Gallegos *et al.*

Support for Claims 127-150:

Claims 127-140 and 141-150 are merely reinstatements of former claims 21-34, and 37-46. Therefore, the claims are supported by the application as originally filed.

Rejection under 35 U.S.C. § 112, first paragraph:

Claims 20, 35, and 36 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description. The Office asserts that the "applicants did not provide any factual evidence to support the statement that basic functional characteristics of a 3' UTR are known .... and applicants did not provide any evidence that these four are representative of the entire genus of genes expressed in *C.elegans* germ line" (page 3 of the Office Action).

Applicants respectfully point out that new claims 136-138 and 148-150 specifically recite a 3' UTR and should not be subject to this rejection.

With respect to claims 20, 35, 36 and new claims 127-135, and 139-147, the applicants respectfully disagree with the rejection. In particular, the representative 3' UTRs used in the experiments to demonstrate the invention are representative of the entire genus as shown by their use in the specification to describe the genus. With regard to the basic functional features of a 3' UTR (*e.g.*, the polyadenylation site, the basic functional features of a 3' UTR are known in the

art, as evidenced by Pesole *et al.* (2000) *Nucleic Acids Res.* 28(1):193-196 and Jareborg *et al.* (1999) *Genome Res.* 9:815–824. The authors of these papers align the known 3' UTRs of many genes. The ability to align a significant number of known 3' UTRs demonstrates (provides objective evidence) that the basic functional characteristics of the 3' UTR are known. These references further demonstrate that functional characteristics beyond the basic characteristics may be identified by sequence comparison. Hence, the specification provides sufficient written description to support the genus of 3' UTRs.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 U.S.C. § 103:

Claims 20, 35, and 36 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Plasterk *et al.*, in view of Vos *et al.*, Van Leunen *et al.* '94[1], Van Leunen *et al.* '93[2], Hackett *et al.* and Gallegos *et al.*

The Office asserts that Plasterk *et al.* discloses methods for integrating desired nucleic acids into other nucleic acid material, including the genome of *C. elegans*. The Office further asserts that the reference teaches Tc1 and its activity in *C. elegans*. The primary example of a transposable element used in Plasterk *et al.*, Tc1, was obtained from *C. elegans*. However, independent claim 20 requires "expressing the transposase gene, such that a transposon in the *C. elegans* genome transposes, causing a mutation in the *C. elegans* germline." Plasterk *et al.* does not disclose expressing the transposase gene to cause a transposon in the *C. elegans* genome to transpose, causing a mutation in the *C. elegans* germline. Instead, the disclosure of Plasterk *et al.* is limited to expression of a Tc1 transposase in somatic cells of *C. elegans*, collection of a nuclear extract from whole animals producing the Tc1 transposase, then use of the collected Tc1 transposase to induce a transposition event *in vitro* (*see*, for example, FIG. 3 and col. 6, line 33 to col. 7, line 26 of Plasterk *et al.*). *In vitro* transposition events were conducted in human cells (*see*, for example, col. 10, line 1 to col. 12, line 7 of Plasterk *et al.*), since the primary purpose of Plasterk *et al.* is directed to gene therapy in humans.

While Gallegos *et al.* studied the post-transcriptional regulatory effects of the *fem-3* UTR, which produces its phenotype in the germline of *C. elegans* (for example, as described on page 6343, second column), the authors do not teach or suggest expressing a transposase gene to cause

an *in vivo* mutation in the *C. elegans* germline. Specifically, Gallegos *et al.* teaches the difficulties of expression in the germline, thereby teaching away from expression of a transgene to produce transposition and causing a mutation in the germline.

Applicants respectfully submit that at the time of the invention the asserted combination of teachings from Plasterk *et al.*, Vos *et al.*, Van Luenen *et al.*[1 or 2], adding the 3' UTR of *fem-3* and using different inducible transcriptional control systems would not have been obvious, since a journal having the reputation of Nature would not have published an obvious combination (Bessereau *et al.* (2001) *Nature* 413:70-74, of record). Hence, the scientific publication by *Nature* of the information contained in the present claims provides evidence that a person of ordinary skill in the art would not have been motivated to combine the cited references.

Moreover, none of the cited references, either alone or in combination, teach or suggest all of the claim elements, including a transposase gene which is operably linked to a regulable expression control element and a 3' untranslated region of a gene that is expressed in the C. elegans germline; and expressing the transposase gene, such that a transposon in the C. elegans genome transposes, causing a mutation in the C. elegans germline. Furthermore, Gallegos *et al.* teaches away from, pointing out the difficulties of, germline expression and Van Luenen *et al.* '93 teaches away from the use of the heat shock promoter for germline expression. Therefore, assuming for the sake of argument that the cited references, either alone or in combination, disclosed all of the claimed elements, there is no motivation to combine the references.

Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

Should questions remain after entry of the amendments and consideration of the applicants remarks that may be addressed in a telephonic conference, the Office is invited to contact the applicants representative at the number provided herein.

Respectfully submitted,

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